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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE		
	Application Number	09/527,558
	Filing Date	March 16, 2000
	First Named Inventor	PFIRRMANN
	Group Art Unit	1623
	Examiner Name	L. MAIER
	Attorney Docket Number	1194-153
Title of the Invention: *ANTICOAGULANT/STERILIZING COMPOSITIONS AND METHODS*		

APPEAL BRIEF

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This is an appeal from the Office Action dated September 19, 2001 in which the Examiner issued a final rejection of claims 1-15 under 35 U.S.C. 103(a). A Notice of Appeal was filed on January 18, 2001.

Real Party in Interest

The owner of the above-referenced patent application and the real party in interest in this appeal is the assignee, Ed. Geistlich Söehne AG für chemische Industrie, of Switzerland.

Related Appeals and Interferences

Applicant is unaware of any other appeals or interferences related to the subject matter of this appeal.

Status of Claims

Claims 1-15 are pending and were finally rejected as a result of the Office Action dated

September 19, 2001. Applicant appeals from the rejection of claims 1-15. The appealed claims are reproduced in the appendix attached hereto. Claims 16-20 have been canceled and claims 21-23 have been withdrawn from consideration.

Status of Amendments

There have been no amendments filed subsequent to the last rejection of the claims as presently pending.

Summary of The Invention

In accordance with the present invention, a composition and method is provided for preventing thrombosis formation on a liquid-contacting surface of a liquid delivery system that is connected to a patient for delivery of a liquid to the patient. The invention comprises a method of preventing thrombosis which utilizes one of two alternative regimens, both of which include the administration of two or more anticoagulants to the patient. The first regimen involves forming a seal in the liquid delivery system with a thrombosis-preventing liquid containing taurolidine, taurultam or a mixture thereof and an additional anticoagulant agent. In an alternative regimen, the liquid-contacting surface of the delivery system is contacted with a solution containing an anticoagulant agent, and thereafter contacted with a solution containing taurolidine, taurultam or a mixture thereof, with the two contacting steps repeated between administration of liquids to the patient.

Claim 1 recites a method of preventing thrombosis formation on a liquid-containing surface of a liquid delivery system comprising one of two alternative regimens selected from the group consisting of:

a) forming a seal in the liquid delivery system between delivery of liquids using a thrombosis-preventing liquid containing taurolidine, taurultam or a mixture thereof and an anti-coagulant agent other than taurolidine or taurultam; and

b) first contacting the surface with a solution containing a thrombosis-preventing amount of an anti-coagulant agent other than taurolidine or taurultam, and thereafter contacting the surface with a solution containing taurolidine, taurultam or a mixture thereof, the surface contacting steps being repeated between delivery of liquids to the patient.

It has been found by the inventors that by forming a seal with a thrombosis-preventing liquid, as set out in the first regimen, effective anti-thrombotic action can be achieved with unexpectedly small quantities of the liquid. Furthermore, with respect to the second regimen, it has been found that the first and second solutions can be sequentially applied avoiding possible interaction between the added anticoagulants and taurolidine/taurultam. The two step application process is then repeated between delivery of liquid to a patient. The invention thus claims a method of either forming a seal with a solution in the liquid delivery system or alternatively contacting the liquid containing surface with two different solutions in a sequential and repetitive manner, both procedures employed to prevent thrombosis formation on the surface of the liquid delivery system.

Issues

The following issues are presented by this appeal:

1) Whether claims 1-15 were properly rejected under 35 U.S.C. 103(a) as unpatentable over Lehner (WO 98/28027) and Reinmuller (U.S. Patent NO. 5,077,281); and

2) Whether claims 1, 14 and 15 were properly rejected under 35 U.S.C. 103(a) as unpatentable over Lehner (WO 98/28027; "Lehner") and Reinmuller (U.S. Patent NO. 5,077,281; "Reinmuller") in view of Ito (U.S. Patent NO. 5,167,960; "Ito").

Grouping of Claims

For purposes of the rejection under 35 U.S.C. § 103(a), Issue 1 set forth above, claims 1 and 13 stand together. Claims 2-12 each stand alone. Claims 14 and 15 stand together.

For purposes of the rejection under 35 U.S.C. § 103(a), Issue 2 set forth above, claim 1 stands alone and claims 14 and 15 stand together.

Argument

1. Claims 1-15 are nonobvious over Lehner and Reinmuller.

Claims 1-15 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Lehner and Reinmuller.

In order for references to render a claim obvious, the references must at least suggest the features of the claim and their combination to a person having ordinary skill in the art. In the present case, the combination of references does not teach or suggest the use of taurolidine or taurultam or a mixture thereof in combination with another anti-coagulant agent to prevent thrombosis formation on a liquid-containing surface of a liquid delivery system by forming a seal in the liquid delivery system. Furthermore, the combination of references does not teach or suggest preventing thrombosis between delivery of liquids by separately contacting taurolidine or taurultam or a mixture thereof in sequential steps, alternating with another anticoagulant, and repeating the two step process between delivery of liquids via the delivery system.

Lehner discloses flushing or sealing a liquid delivery system with taurolidine or taurultam for the purpose of combating infection or sepsis. Reinmuller discloses a method for the prevention of thrombosis, teaching the use of taurolidine or taurultam as an anticoagulant contacted with a surface and further suggesting that these compounds may be used **together** with known anti-coagulants such as heparin. Reinmuller discloses that a *single contact* with taurolin is continuously effective to prevent coagulation on a surface after implantation. *See* Col. 4 lines 41-47.

Lehner does not teach or suggest preventing thrombosis formation. Reinmuller does not teach or suggest a method which would encompass flushing or sealing a liquid in or on the surface of a liquid delivery system. Reinmuller also does not teach or suggest a two step process wherein the liquid containing surface of the delivery system is contacted *first* with an anticoagulant and *second* with a taurolidine or taurultam solution, wherein the two step process is repeated between periods of delivery of a liquid to a patient. In contrast to these two references, the present claims are to a method whereby thrombosis is prevented by (1) sealing a delivery system with a solution containing taurolidine or taurultam combined with an additional coagulant to prevent thrombosis formation or (2) first contacting the surface of the system with a solution containing a thrombosis-preventing amount of an anticoagulant agent other than taurolidine or taurultam and then contacting the surface with a solution containing taurolidine, taurultam or a mixture thereof, wherein the contacting steps are repeated between delivery of liquids to the patient.

Applicable case law holds that in order to render a claim obvious, the prior art must teach

or suggest all of the features of the claim and their combination to a person having ordinary skill in the art. The test for obviousness under 35 U.S.C. ¶103 (a) is set forth by the United States Supreme Court in *Graham v. John Deere, Co.*, 383 U.S. 1, 17-18 (1966). As mandated therein, in an obviousness determination under ¶103, the scope and content of the prior art are to be determined, the differences between the prior art and the claims at issue are to be ascertained and the level of ordinary skill in the pertinent art resolved.

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

Since the combination of references cited by the Examiner does not teach or suggest any modification whatsoever of the prior art to arrive at the present invention, a finding of obviousness could only arise through some motivation to combine the references. When the motivation to combine the teachings of the references is not immediately apparent, it is the duty of the examiner to explain why the combination of the teachings is proper. *Ex parte Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Inter. 1986). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior

art, not in applicant's disclosure. *In re Vaeck,* 947 F.2d at 493.

Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577 (Fed. Cir. 1984). A suggestion, teaching or motivation to combine the prior art references is an "essential evidentiary component of an obviousness holding." *C.R. Bard, Inc. v. MP3 Sys., Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998). Furthermore, the suggestion must be clear and particular; "broad conclusory statements about the teaching of multiple references, standing alone, are not 'evidence'". *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1125 (Fed. Cir. 2000). In reversing a finding of obviousness by the Board of Patent Appeals and Interferences, the Federal Circuit recently noted that "[t]he need for specificity **pervades** this authority." *In re Lee*, 277 F.3d 1338, 1343, 61 U.S.P.Q. 2d 1430, 1433 (Fed. Cir. 2002) (*emphasis added; citing In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000): "particular findings must be made as to the reason the skilled artisan , with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.") In particular, evidence of obviousness must provide an " impetus . . . to cause one skilled in the art to combine the teachings of the references to make the proposed modification." *Ex parte Levengood*, 28 U.S.P.Q.2d 1300, 1301, n.2 (*citing In re Albrecht*, 185 U.S.P.Q. 585 (C.C.P.A. 1975)). The combination of cited art must provide evidence of the motivating force which would motivate one to do what the applicant has done.

The issue is not whether the combination could have been done, but whether the contents of the prior art references provide motivation to make the combination. Accordingly, in the

present case, the PTO cannot establish obviousness by locating references which describe various aspects of Appellants' invention without also providing evidence that one skilled in the art would have been motivated to combine the separate components. Based on the pervasive authority in this area, it is well-established that the Examiner cannot merely assert the possibility of the combination.

In the present case, there is no motivation in the prior art for the proposed combination. First, Lehner does not serve the same purpose or function as the present invention. Lehner is concerned with the prevention of infection or sepsis, while Reinmuller and the present invention are directed to the prevention of thrombosis. There would be no motivation or suggestion for one seeking to prevent sepsis to look to the anti-thrombolytic teachings of Reinmuller. There would similarly be no motivation or suggestion for one seeking to prevent thrombosis to look to the anti-microbial teachings of Lehner.

Assuming, *arguendo* that the skilled artisan examined Reinmuller in an effort to improve the teachings of Lehner, regardless of the inherent anti-coagulant activities of taurolidine or taurultam, there is nothing in Reinmuller to suggest adding an additional anticoagulant to prevent sepsis. In analogous manner, if the skilled artisan examined Lehner in an effort to improve Reinmuller, nothing in Lehner would suggest application of an antimicrobial seal in order to prevent thrombosis. Furthermore, nothing in Lehner would suggest repeating a two step application process between delivery of liquids with a liquid delivery system.

It is not entirely clear from the Examiner's actions why a person having ordinary skill in the art would consider combining the teachings of Lehner and Reinmuller. In fact, there is

simply no motivation to combine them. There is nothing in either reference to suggest the desirability of making the combination. The first attempt at such an explanation was an assertion that inherent in Lehner is the prevention of thrombosis. Paper No.3, pg. 4. Then, in finally rejecting the claims, the Examiner asserted the following:

> "It would have been obvious to one having ordinary skill in the art to have used a solution of taurolidine, taurultam, or a mixture thereof and an anticoagulant agent, such as heparin or courmarin, other than taurolidine or taurultam to prevent thrombosis formation in a liquid delivery system either by using the solution to flush the system or by sealing the system with the solution. It would be within the scope of the artisan to determine the optimum time for treating the system and the optimum concentrations for the method with routine experimentation." Paper No.10, pg 4.

The Examiner appears to rely only on the fact that taurolin derivatives exhibit both infection fighting and anticoagulant properties for the claim that the present invention would be obvious to a person having ordinary skill in the art. However, no combination of the prior art would result in the present invention as specified in the first regimen of claim 1, since none of the prior art suggest sealing a delivery system with a solution containing taurolidine or taurultam **combined with** an additional coagulant, whether to prevent sepsis or thrombosis. The second regimen of claim 1 discloses a method of preventing thrombosis in a liquid-delivery system by **first contacting** the surface with a solution containing a thrombosis-preventing amount of an anticoagulant agent other than taurolidine or taurultam, **then contacting** the surface with a solution containing taurolidine, taurultam or a mixture thereof and **repeating** the contacting steps

between delivery of liquids to the patient.

Neither reference suggests repeating such a two-step process between administration of liquids to the patient to prevent thrombosis. In fact, as the examiner pointed out, Reinmuller teaches that a *single contact* with taurolin is continuously effective to prevent coagulation on a surface after implantation. See Col. 4 lines 41-47. Thus, Reinmuller actually teaches away from the repetitive two-step process as set out in the second regimen. After being led away from the present invention by the teachings of Reinmuller, nothing in Lehner would return a person having ordinary skill in the art to the concept of contacting the surface with two distinct anticoagulant compositions in sequence, repeating the process between delivery of a liquid.

Here, the Examiner has not pointed to any evidence, either in the references or the general knowledge of the prior art, of a suggestion or motivation to combine the references as set forth in the claims. The broad conclusory statement by the Examiner that it would be obvious to combine these two references, either based on what is taught therein, or based on the level of ordinary skill in the art, is completely unsupported.

As the Federal Circuit has noted in *In re Rouffet*, 47 U.S.P.Q. 2d 1453 (Fed. Cir. 1998) "...an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention." *Id.* at 1457. The court in Rouffet went on to state, "[t]o prevent the use of

hindsight based on the invention to defeat patentability of the invention, this court requires the examiner to show a motivation to combine the references that create the case of obviousness."*Id.* at 1457-58.

Claim 1 is the only independent claim pending. Claim 13 recites a method as in claim 1 wherein said solution or liquid containing taurolidine, taurultam or a mixture thereof contains from about 0.5 to about 3% by weight of taurolidine, or from about 1 to about 7.5% by weight of taurultam. These claims stand rejected without any well reasoned or valid explanation as to what would provide motivation to a person having ordinary skill in the art to combine the teachings of Lehner and Reinmuller to arrive at the presently claimed invention as claimed in claim 1 and dependent claim 13. It is submitted that the Examiner's assertion of obviousness based on these references is improper because it is supported by no more than the application of hindsight to the prior art, in light of the Applicant's own disclosure.

Claim 5 depends from claim 1 and further recites a method wherein, when first contacting the surface with the anticoagulant solution, the surface is flushed with the solution. Claim 5 is nonobvious over a combination of Lehner and Reinmuller for all of the reasons applied to claim 1 above. Furthermore, claim 5 is nonobvious over a combination of Lehner and Reinmuller for the separate and distinct reason that a combination of references does not teach or suggest a method of preventing thrombosis on a liquid-contacting surface wherein the surface is flushed with the anticoagulant solution when first contacting the surface.

Claim 9 depends from claim 1 and recites a method wherein the anticoagulant-containing solution is contacted with said surface by injecting the solution into the liquid delivery containing

solution and then removing the anti-coagulant containing solution from the delivery system. Claim 9 is nonobvious over a combination of Lehner and Reinmuller for all of all of the reasons applied to claim 1 above. Furthermore, claim is nonobvious over a combination of Lehner and Reinmuller for the separate and distinct reason that a combination of these references does not teach or suggest a method of preventing thrombosis on a liquid-contacting surface wherein the anticoagulant-containing solution is contacted with said surface by injecting the solution into the liquid delivery containing solution and then removing the anti-coagulant containing solution from the delivery system.

Claims 2, 6 and 10 depend from claims 1, 5 and 9 respectively and further recite a method for preventing thrombosis wherein the thrombosis preventing solution is contacted with the surface of the liquid delivery system for at least about 1 hour. Claims 2, 6 and 10 are nonobvious over a combination of Lehner and Reinmuller for all of the reasons applied to claim 1 above. Furthermore, claims 2, 6 and 10 are nonobvious over a combination of Lehner and Reinmuller for the separate and distinct reason that a combination of these references does not teach or suggest a method as in claim 1, 5 or 9, wherein the thrombosis preventing solution is contacted with the surface of the liquid delivery system for at least about 1 hour.

Claims 3, 7 and 11 depend from claims 1, 5 and 9 respectively and further recite a method for preventing thrombosis wherein said solution or liquid containing taurolidine, taurultam or mixture thereof is sealed in said delivery system for a period of at least 12 hours. Claims 3, 7 and 11 are nonobvious over a combination of Lehner and Reinmuller for all of the reasons applied to claim 1 above. Furthermore, claims 3, 7 and 11 are nonobvious over Lehner and

Reinmuller for the separate and distinct reason that a combination of these references do not teach or suggest a method for preventing thrombosis as in claim 1, 5 or 9 wherein said solution containing taurolidine, taurultam or mixture thereof is sealed in said delivery system for a period of at least 12 hours.

Claims 4, 8 and 12 depend from claims 1, 5 and 9 respectively and recite a method for preventing thrombosis wherein said taurolidine, taurultam or a mixture thereof which is sealed in said delivery system is replaced at least about daily. Claims 4, 8 and 12 are nonobvious over a combination of Lehner and Reinmuller for all of the reasons applied to claim 1 above. Furthermore, claims 2, 6 and 10 are nonobvious over a combination of Lehner and Reinmuller for the separate and distinct reason that a combination of these references does not teach or suggest a method for preventing thrombosis wherein said taurolidine, taurultam or a mixture thereof which is sealed in said delivery system is replaced at least about daily.

Claims 14 depends from claim 1 and recites a method wherein the anticoagulant solution is selected from the group consisting of sodium citrate, aprotinin, hirudin, desirudin, danaparoid, danaparoid-sodium, heparin, pentosan, pentosanpolysulfate-sodium, ticlopidine, clopidogrel, and mixtures thereof. Claim 15 depends from claim 14 and recites a method wherein said anticoagulant is present in an amount within a range of from about 0.1-10mg. Claims 14 and 15 are nonobvious over a combination of Lehner and Reinmuller for all of the reasons applied to claim 1 above. Furthermore, claims 14 and 15 are nonobvious over a combination of Lehner and Reinmuller for the separate and distinct reason that a combination of these references does not teach or suggest a method for preventing thrombosis wherein the anticoagulant solution is

selected from the group consisting of sodium citrate, aprotinin, hirudin, desirudin, danaparoid, danaparoid-sodium, heparin, pentosan, pentosanpolysulfate-sodium, ticlopidine, clopidogrel, and mixtures thereof or is present in an amount within a range of from about 0.1-10 mg.

Based on the foregoing, the Applicant respectfully submits that claims 1-15 of the present application are nonobvious over a combination of Lehner and Reinmuller and requests withdrawal of this rejection.

2. Claims 1, 14 and 15 are nonobvious over Lehner and Reinmuller in view of Ito

Claims 1, 14, and 15 were also rejected under 35 U.S.C. §103(a) as being unpatentable over Lehner and Reinmuller further in view of Ito *et al.*, U.S. 5,167,960 (Ito). The Examiner has cited Ito for disclosing the use of hirudin or a hirudin derivative that can be utilized to inhibit thrombosis on implantable and extracorporeal devices. The Examiner is of the opinion that Ito teaches anticoagulants including hirudin and its derivatives and further alleges that it would have been obvious to substitute any art-disclosed anticoagulant and further that a person having ordinary skill in the art could readily determine optimum time and concentrations of their administration.

Regardless of the disclosure of Ito as applied by the Examiner, this reference does nothing to remedy the basic deficiencies of Lehner and Reinmuller discussed above. Accordingly, no combination of the cited references would result in the method as set out in claim 1. Thus, for the same reasons as applied to claim 1 in the previous argument, it is respectfully submitted that claim 1 is nonobvious over a combination of Lehner, Reinmuller and Ito.

Claims 14 and 15 depend from claim 1 and further recite a method for preventing thrombosis wherein the anticoagulant solution is selected from the group consisting of sodium citrate, aprotinin, hirudin, desirudin, danaparoid, danaparoid-sodium, heparin, pentosan, pentosanpolysulfate-sodium, ticlopidine, clopidogrel, and mixtures thereof or is present in an amount within a range of from about 0.1-10 mg. For the same reasons as applied to claim 1, claims 14 and 15 are nonobvious over a combination of Lehner, Reinmuller and Ito. Furthermore, claims 14 and 15 are nonobvious over a combination of Lehner, Reinmuller and Ito for the separate and distinct reason that a combination of these references does not teach or suggest a method for preventing thrombosis as in claim 1 wherein the anticoagulant solution is selected from the group consisting of sodium citrate, aprotinin, hirudin, desirudin, danaparoid, danaparoid-sodium, heparin, pentosan, pentosanpolysulfate-sodium, ticlopidine, clopidogrel, and mixtures thereof or is present in an amount within a range of from about 0.1-10 mg. Ito provides nothing to remedy the deficiencies of Lehner and Reinmuller, as pointed out above.

Based on the foregoing, the Applicant submits that claims 1, 14, and 15 are nonobvious over Lehner and Reinmuller in view of Ito and requests withdrawal of this rejection.

CONCLUSION

In view of the foregoing, Applicant respectfully submits that all grounds of rejection of claims 1-15 are submitted to be unsupportable on the record and thus improper. The Honorable Board is therefore respectfully requested to reverse all grounds of rejection and to direct the passage of this application to issue.

Respectfully submitted,

By: 

Michael J. Moran
Attorney for Applicants
Registration No.: 42,013
ROTHWELL, FIGG, ERNST & MANBECK, p.c.
1425 K Street N.W., Suite 800
Washington, D.C. 20005
Telephone: (202)783-6040

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APPENDIX

1 (Amended). A method of preventing thrombosis formation on a liquid-containing surface of a liquid delivery system, the liquid delivery system being connected to a patient for delivery of a liquid to said patient, the method comprising a regimen selected from the group consisting of:

A) forming a seal in the liquid delivery system between delivery of liquids using a thrombosis-preventing liquid containing taurolidine, taurultam or a mixture thereof, said thrombosis-preventing liquid further containing an anticoagulant agent other than taurolidine or taurultam, and

B) first contacting surface with a solution containing a thrombosis-preventing amount of an anticoagulant agent other than taurolidine or taurultam, and thereafter contacting said surface with a solution containing taurolidine, taurultam or a mixture thereof, said surface contacting steps being repeated between delivery of liquids to said patient.

2. The method of claim 1 wherein the solution or liquid containing taurolidine, taurultam or mixture thereof is contacted with said surface for at least about 1 hour.

3. The method of claim 2 wherein said solution or liquid containing taurolidine, taurultam or mixture thereof is sealed in said delivery system for a period of at least 12 hours.

4. The method of claim 3 wherein said solution or liquid containing taurolidine, taurultam or mixture thereof which is sealed in said delivery system, is replaced at least about daily.

5. The method of claim 1 wherein, when first contacting said surface with the anticoagulant solution, said surface is flushed with said anticoagulant-containing solution.

6. The method of claim 5 wherein the solution containing taurolidine, taurultam or a mixture

thereof is contacted with said surface for at least about 1 hour.

7. The method of claim 6 wherein said solution containing taurolidine, taurultam or a mixture thereof is sealed in said delivery system for a period of at least about 12 hours.

8. The method of claim 7 wherein the solution containing taurolidine, taurultam or a mixture thereof which is sealed in said delivery system is replaced at least about daily.

9. The method of claim 1 wherein the anticoagulant-containing solution is contacted with said surface by injecting the anticoagulant-containing solution into said liquid delivery system and then removing said anticoagulant-containing solution from said liquid delivery system.

10. The method of claim 9 wherein the solution containing taurolidine, taurultam or a mixture thereof is contacted with said surface for at least about 1 hour.

11. The method of claim 10 wherein the solution containing taurolidine, taurultam or a mixture thereof is sealed in said delivery system for a period of at least about 12 hours.

12. The method of claim 11 wherein the solution containing taurolidine, taurultam or a mixture thereof which is sealed in said delivery system, is replaced at least about daily.

13. The method of claim 1 wherein said solution or liquid containing taurolidine, taurultam or a mixture thereof contains from about 0.5 to about 3% by weight of taurolidine, or from about 1 to about 7.5% by weight of taurultam.

14. The method of claim 1 wherein said anticoagulant agent is selected from the group consisting of sodium citrate, aprotinin, hirudin, desirudin, danaparoid, danaparoid-sodium, heparin, pentosan, pentosanpolysulfate-sodium, ticlopidine, clopidogrel, and mixtures thereof.

15. The method of claim 14 wherein said anticoagulant is present in an amount within a range of from about 0.1-10mg.